REMARKS

Claims 1-27 are pending and under consideration in the above-identified application. Claims 28-59 have been cancelled previously without prejudice. Claims 1, 17, 20 and 21 have been amended herein.

Base claims 1 and 20 have each been amended to insert the phrase "a combination of" to provide express antecedent basis for the term "combination" and convey with clarity that the "combination" refers back to the least two compounds that modulate the activity of one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs). The amendments to claims 1 and 20 is supported throughout the application, for example, at page 2, lines 13-20. Accordingly, no new matter is introduced by the amendments to claim 1 and 20. Claims 17 and 21 have been rewritten without addition of new matter to clarify the antecedent basis for the term "modulation effect." Applicant respectfully requests entry of the amendments.

Rejections under 35 U.S.C. § 112, first paragraph

A. Written Description

The rejection of claims 1-27 under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide adequate written description of the invention is respectfully traversed. The Office Action cites *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991) and *Regents of University of California v. Eli Lilly & Co.*, 119 F.3d

1559, 43 USPQ2d 1398 (Fed. Cir.1997) to support the assertion that Applicant has not identified a representative number of compounds within the claimed genus. For the reasons that follow, Applicant respectfully submits that the Examiner misapplies the written description case law and that the specification provides adequate written description of the claimed invention.

The Federal Circuit has indicated that a rejection for lack of written description is appropriate where the claims cannot be practiced based on the specification, even considering the knowledge of one skilled in the art. *See, University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (2004). In *Rochester*, the Federal Circuit recently indicated that the issue for written description is not simply whether claimed compounds are disclosed, but also whether such claimed compound were known in the art. *See Id.* Applicant respectfully submits that the skilled person with knowledge of the art and familiar with the specification, would be able to envision compounds suitable for inclusion in a composition of the invention. Applicant respectfully submits that the claims under consideration can be practiced based on the specification and considering the knowledge of one skilled in the art. Furthermore, the compounds suitable for inclusion in the claimed compositions were known in the art and the skilled person familiar with the specification would have known of such compounds.

Briefly, base claim 1 is directed to a composition of compounds effective for treating a pathology, the composition that includes a combination of at least two compounds that modulate the activity of one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs), wherein each compound

modulates the activity of at least one target molecule associated with one or more SNPs, and wherein the combination is effective for at least one patient having the pathology. Base claim 20 is directed at a composition of compounds effective for treating a pathology, said composition comprising at least two compounds that modulate the activity of at least one target molecule associated with at least one SNP, wherein said combination is effective for at least one patient having said pathology.

The specification provides written description of compounds suitable for inclusion in a composition of the invention by indicating that the term is used in reference to a pharmaceutically active agent used to effect a physiological change in treating a pathology (specification, page 4, lines 17-23)). The specification teaches that exemplary compounds can be chosen from drugs, pharmaceutically active natural products or dietary supplements, or any other type of compound (i.e., agent) useful in treating a pathology (specification, page 4, lines 24-27). It is further described that, preferably, one or more of the compounds in the composition will be targeted toward treating a subset of the total population of patients with a pathology, in which the constituents of this subset have related or identical genetic profiles (specification, page 4, lines 27-31). The specification further teaches that a compound targeted toward such a subset of the total population refers to a compound directed to modulating the activity of one or more target molecules that play a role in the pathology, wherein the one or more target molecules are associated with one or more genetic variations characteristic of that subset of the population and can play a role in the symptoms, etiology, side-effects, progression of treatment, and the like, of a pathology (specification, page 4, line 31, to page 5, line 8). It is also taught that an invention composition of compounds preferably can include specific amounts of two or

more compounds, combined for the purpose of effectively treating an optimum percentage of patients with a pathology while maintaining little or no toxicity. The specification provides further written description to the skilled person by teaching that a compound that is effective against a target molecule associated with one or more particular genetic variations refers to the ability of a compound to modulate the activity of a target molecule that plays a role in the symptoms, etiology, complications or treatment of a pathology (specification, page 7, lines 8-14).

In view of the above, Applicant respectfully submits that the skilled person with knowledge of the art and familiar with the specification, would be able to envision compounds suitable for inclusion in a composition of the invention, for example, a drug, pharmaceutically active natural product or dietary supplement known to be useful in treating a pathology. Accordingly, Applicant respectfully requests removal of the rejection of claims 1-27 under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide adequate written description of the invention.

B. Regarding Enablement

The rejection of claims 1-27 under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification so as to enable one skilled in the art to practice the claimed invention is respectfully traversed.

The Office Action asserts that, while enabling for compositions consisting of a specific HIV vaccine of U.S. Patent No. 5,846,546, and the HBV antibody composition of U.S. Patent No. 5,648,077, the specification does not reasonably provide enablement

for compositions containing two or more compounds that are to be used to treat any pathology, wherein the compounds modulate the activity of one or more target compounds associated with any SNP (current Office Action, page 7, first full paragraph). Applicant respectfully submits that the specification enables the full scope of claims 1-27.

Applicant submits that any use that reasonably correlates with the scope of the claim is sufficient to preclude a rejection for nonenablement based on how to use. To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *Genentech, Inc. v. Novo Nodisk A/S*, 108 F.3d 1361, 1365, 42 U.S.P.Q.2d 1001, 1004 (Fed. Cir. 1997), *see also* MPEP §2164.01(c), fourth paragraph. In *Amgen, Inc. v. Hoechst Marion Roussel, Inc*, 232 F.3d 905 (Fed.Cir. 2000), the Federal Circuit clarified the enablement requirement:

The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation."

Id. (citing *Genentech, Inc. v. Novo Nordisk, A/S,* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991))

In *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998), the Federal Circuit clearly stated that routine experimentation does not constitute undue experimentation:

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Id. (Emphasis added) (citing *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d at 1564, 37 U.S.P.Q.2d at 1623); see also *In re Wands*, 858 F.2d at 736-40, 8 U.S.P.Q.2d at 1403-07.

The claims at issue recite a composition of compounds that modulate the activity of one or more target molecules associated with one ore more SNPs, each compound capable of modulating at least one target molecule associated with one or more SNPs. A component compound of a composition of the invention modulates a target molecule associated with one or more SNPs. The specification teaches that, for a particular pathology, one or more SNPs can be correlated with the symptoms, etiology, side-effects or progression of treatment of that pathology as well as with the efficacy, or toxicity, or both, of a compound used for treating the pathology (specification as filed, page 9, lines 3-9). As further guidance to the skilled person, the specification teaches that patients with a particular pathology have a unique combination of genetic variations correlated with a pathology that can be referred to as the genetic profile or genotype (specification as filed, page 9, lines 20-29).

With regard to identification of a SNP, the specification provides teachings and guidance by disclosing that a SNP can be identified by finding a difference in the nucleotide sequence of an individual compared to the most common nucleotide sequence of the overall population (specification as filed, page 10, lines 17-20). The specification further describes and provides patent citations for methods for SNP identification that are well known in the art, including hybridization stability methods such as SSCP, where the hybrids are identified, for example, by electrophoretic analysis, denaturing HPLC or addressable DNA array hybridization (specification as filed, page 10, lines 17-26). The specification provides additional guidance to the skilled person by disclosing that a perturbation resulting from the hybrid instability can be exploited to detect SNPs by its impact on enzymatic reactions such as restriction endonucleases (RFLP), allele-specific oligonucleotide ligation, allele-specific cleavage, allele-specific PCR, and allele-specific LCR (specification as filed, page 10, line 26, to page 11, line 2). In addition, the specification discloses other methods for detecting SNP genetic variations including use polymerase-dependent primer extension techniques such as GBA which uses single nucleotide extension or limited extension from a specific primer for analysis by, for example, mass spectrometry (specification as filed, page 11, lines 2-8). The specification further teaches that correlation of data to identify a site of a genetic variation such as a SNP can be carried out by sequence comparison of the results of the taught assays for multiple individuals and provides several citations to the skilled person that provide further guidance on methods for sequence comparison (specification as filed, page 11, lines 8-13). Thus, the specification provides considerable teachings and guidance to the skilled person for detection of SNPs.

With regard to establishing a correlation, the specification teaches that certain genetic variations are correlated with a pathology or treatment of a pathology, for example, the SNP encoding the change from normal hemoglobin to sickle hemoglobin in sickle cell anemia (specification as filed, page 11, lines 13-17). The specification further discloses that methods for using a variety of patient determinants such as genetic variations to establish if one or more determinants are correlated with a pathology, or if one or more determinants are correlated with treatment of a pathology, are known in the art and provides a number of citations to patents and international patent publications that are incorporated by reference for their teachings with regard to establishing such correlations (specification as filed, page 11, lines 17-24).

Applicant further respectfully submits that methods for identifying a target molecule associated with one or more SNPs that plays a role in the symptoms, etiology, complications or treatment of a pathology were known in the art at the time the present application was filed. In this regard, Applicant has previously provided publications by Hijikata et al., *Intervirology* 43(2):124-127 (2000) and Lambert et al., *J. Med. Genet.* 38(6):353-355(2001), respectively. Hijikata et al. report the identification of a SNP in the MxA gene promoter correlated with the response to hepatitis C patients to interferon treatment. This reference describes the identification, via routine methods, of a target molecule associated with a SNP that plays a role in the treatment of a pathology. Lambert et al. describe a SNP in the presenilin 1 promoter that is associated with an increased risk of Alzheimer's disease and an increased risk of Abeta protein load in the brain. This reference describes identification, via routine methods, of two target molecules associated with a SNP that play a role in the symptoms of a pathology.

Applicant respectfully maintains that these references clearly communicate that the identification of a target molecule that is associated with one or more SNPs that plays a role in the symptoms, etiology, complications or treatment of a pathology were known in the art at the time the present application was filed.

With regard to compounds effective against a target molecule associated with one ore more SNPs, the specification teaches that the compound can modulate the activity of a target molecule that plays a role in the symptoms, etiology, complications or treatment of a pathology as well as can modulate the activity of a target-protein associated with one or more genetic variations that plays a role in the symptoms, etiology, complications or treatment of a pathology (specification as filed, page 7, lines 9-14). The specification further discloses as an example a protease normally having a glutamate at a position near the active site that can have increased proteolytic activity as a result of a single nucleotide polymorphism arising in which the glutamate is changed to alanine, resulting in a particular SNP playing a role in a pathology caused by increased proteolytic activity (specification as filed, page 7, lines 17-24). A compound, such as a protease inhibitor, can be effective against a protease target protease with this SNP by inhibiting the proteolytic activity of the protease. Armed with the guidance provided by the specification, the skilled person would have been able to prepare a composition encompassing at least two compounds, for example protease inhibitors, after confirming via routine methods not requiring undue experimentation, that each compound modulates the activity of a target molecule, for example a protease, that is associated with one or more SNPs.

In addition to the teachings and guidance provided by the specification with regard to identifying a SNP in a target molecule, identifying a compound that modulates the activity of a target molecule associated with one or more SNPs, and establishing a correlation between a pathology or treatment thereof and a genetic variation, the specification discloses an algorithm for determining the efficacy and/or toxicity of a combination of two or more compounds for a population of patients having a pathology (specification, page 33, line 22, to page 34, line 10). Further with regard to determining efficacies, the specification exemplifies optimization of efficacy for five compounds with additive efficacies for five equally populated as well as for two compounds with additive efficacies for two variably populated genotypes (specification, Examples I and II, pages 36-44). Thus, the specification exemplifies determination and optimization of efficacy for a composition of the invention, teaching the skilled person both how to make and how to use the claimed compositions.

In view of the above, Applicant submits that the specification provides sufficient teachings to enable those in the art to can make and use the invention compositions without undue experimentation. Accordingly, Applicant respectfully requests withdrawal of the objection to the specification and corresponding rejection of claims 1-27 under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification so as to enable one skilled in the art to practice the claimed invention.

Rejections under 35 U.S.C. § 112, second paragraph

The rejection of claim 1-27 under 35 U.S.C.§ 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention.

Applicant submits that the U.S. Court of Appeals for the Federal Circuit has indicated in its numerous decisions on the issue that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *See, e.g., In re Marosi*, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 221 U.S.P.Q. 1 (Fed. Cir. 1984); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983); and *Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999) (district court failed to consider the knowledge of one skilled in the art when interpreting the patent disclosure).

> The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe. That determination requires a construction of the claims according to the familiar canons of claim construction.

All Dental Prodx, LLC v. Advantage Dental Prods., 309 F.3d 774, 779-80, 64 USPQ2d 1945, 1949 (Fed. Cir. 2002) (citations omitted).

The determination of whether a claim is invalid as indefinite "depends on whether those skilled in the art would understand the scope of the claim when the claim is read in

light of the specification." *See N. Am. Vaccine, Inc. v. Am. Cyanamid Co.*, 7 F.3d 1571, 1579 (1993) (citation omitted).

With regard to the assertion various claim terms are indefinite, Applicant respectfully submits that each of the terms, viewed by the skilled person in light of the specification and what was known in the art, is sufficiently clear and definite to meet the requirements of paragraph 112.

According to the Federal Circuit, "[M]athematical precision is not required--only a reasonable degree of particularity and definiteness." *Exxon v. US*, 265 F.3d 1371, 1381; 60 U.S.P.Q.2d 1272, 1279 (Fed. Cir. 2001).

Regarding the phrase "said combination"

The Office Action asserts that claims 1-27 are indefinite over the recitation of "said combination" because this phrase lacks proper antecedent basis. It is alleged that, while the claims previously refer to two compounds, the claims do not previously refer to a combination.

Applicant submits that this rejection has been rendered moot by the amendment to base claims 1 and 20, which now clarify that a composition of compounds encompasses a combination of at least two compounds. Applicant notes that this amendment, which merely clarifies the antecedent basis, does not alter the claim scope. Accordingly, removal of this ground for rejection is respectfully requested.

Regarding "target molecules associated with one or more SNPs"

The Office Action further asserts that claims 1-27 are indefinite over the recitation of "target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs)." The Office Action alleges that, while the specification teaches that a target molecule associated or correlated with a particular SNP is a molecule that can be functionally distinguished in its structure, activity, concentration, compartmentalization, secretion, and the like, as a result of such genetic variation, this teaching does not provide a clear and complete definition for what is intended to be encompassed by target molecules associated with SNPs.

Applicant respectfully submits that, when viewed by the skilled person in light of the specification and what was known in the art, the phrase "target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs)" is sufficiently clear and definite to meet the requirements of paragraph 112. In this regard, the specification passage cited in the Office Action makes it clear to the skilled person that a target molecule is considered associated with a SNP if the target molecule has a measurable characteristic, which changes in correlation with the presence or absence of a SNP. A skilled person familiar with the specification would further understand that the characteristic can be structure, activity, concentration, compartmentalization, secretion, and the like, and that the change can be qualitative or quantitative. Accordingly, the phrase "target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs)" is submitted to be sufficiently clear and definite to meet the requirements of

paragraph 112 when viewed by the skilled person in light of the specification. Accordingly, removal of this ground for rejection is respectfully requested.

Regarding the term "corresponding"

Claim 7 is alleged to be indefinite over the recitation of "corresponding" to describe the relationship between a target molecule and a SNP. It is allegedly unclear if the term describes the relationship between the target molecule and the SNP and whether the position constitutes the location of the polymorphism in a nucleic acid or protein or if the position defines some other unstated relationship between the polymorphism and the target molecule. Applicant respectfully submits that the term corresponding should be viewed in context of the phrase "position corresponding," which makes clear to the skilled person that the position is that of the SNP or an amino acid residue encoded by a codon that encompasses said SNP. Applicant respectfully submits that, when viewed by the skilled person in light of the specification and what was known in the art, the phrase "position corresponding" is sufficiently clear and definite to meet the requirements of paragraph 112. Accordingly, removal of this ground for rejection is respectfully requested.

Regarding the term "interacts"

It is further alleged unclear as to what is intended to be encompassed by "interacts," as this term supposedly does not clearly define the relationship between the compound and the target molecule. Here, the Office Action indicates that it is unclear as to whether the molecules bind to one another or if the molecules indirectly alter the

activity or expression of one another. Applicant respectfully submits that the skilled artisan, viewing this term in the context of the specification, would understand that the compound can interact with the target molecule in a direct or an indirect manner. Accordingly, removal of this ground for rejection is respectfully requested.

Regarding the term "modulation effects"

Claims 17 and 21 are alleged to be indefinite over the recitation of "the modulation effects" because this phrase lacks proper antecedent basis since the claims do not previously refer to a modulation effect.

Applicant submits that this rejection has been rendered moot by the amendment to base claims 17 and 21, which now clarify antecedent basis for the recited modulation effects. Applicant notes that the amendments to claim 17 and 21, which merely clarify the antecedent basis, do not alter the claim scope. Accordingly, removal of this ground for rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

The rejection of claims 1-27 under 35 U.S.C. §102(a) or 102 (e) as allegedly anticipated by United States Patent No. 5,846,546, to Hurwitz et al. respectfully is traversed. The Office Action asserts that Hurwitz discloses HIV vaccines that modulate the activity of target molecules containing SNPs by inducing humoral or cellular immune responses against the target molecule. The vaccines preferably contain about 10 to 100 recombinant viruses each expressing a different HIV env protein variant (EPV). Each

EPV contains a point mutation present in a different strain of HIV, which the Office Action equivocates to SNPs.

When lack of novelty is based on a printed publication that is asserted to describe the same invention, a finding of anticipation requires that the publication describe all of the elements of the claims. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1349, 48 U.S.P.Q.2d 1225, (Fed. Cir. 1998) (quoting *Shearing v. Iolab Corp.*, 975 F.2d 1541, 1544-45, 24 U.S.P.Q.2d 1133, 1136 (Fed. Cir. 1992)). To establish a *prima facie* case of anticipation, the Examiner must show that the single reference cited as anticipatory art describes all the elements of the claimed invention.

Briefly, base claim 1 is directed to a composition of compounds effective for treating a pathology, the composition that includes a combination of at least two compounds that modulate the activity of one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs), wherein each compound modulates the activity of at least one target molecule associated with one or more SNPs, and wherein the combination is effective for at least one patient having the pathology. Base claim 20 is directed at a composition of compounds effective for treating a pathology, said composition comprising at least two compounds that modulate the activity of at least one target molecule associated with at least one SNP, wherein said combination is effective for at least one patient having said pathology.

The Office Action fails to particularly point out each of the elements claimed by in the invention that are allegedly described in Hurwitz. The vaccines appear to represent the composition of compounds effective for treating a pathology, however they also

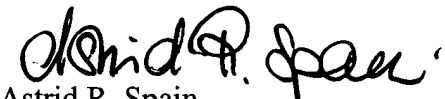
appear to be representing the one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs). The Examiner has not pointed out with particularity where the Hurwitz et al. patent describes each and every element of the claimed invention. Accordingly, the Office has not met the burden of establishing a prima facie case of anticipation. Accordingly, withdrawal of the rejection of claims 1-27 under 35 U.S.C. §102(a) or 102 (e) as allegedly anticipated by United States Patent No. 5,846,546, to Hurwitz et al. respectfully is respectfully requested.

CONCLUSION

In light of the Remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney. To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

MCDERMOTT WILL & EMERY LLP



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